(FILE 'HOME' ENTERED AT 21:32:56 ON 27 JUL 2009)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH, LIFESCI' ENTERED AT 21:33:55 ON 27 JUL 2009

- L1 169 S (PEPTIDE OR PROTEIN OR POLYPEPTIDE OR ANTIBODY) (5A)BIND? (4A) L
 L2 4340 S (LIGAND OR LIPOPROTEIN OR PEPTIDE OR PROTEIN OR POLYPEPTIDE O
- L3 23165 S ADENO-ASSOCIATED(3A)VIRUS OR AAV
- L4 4344 S L1 OR L2
- L5 7 S L3 AND L4
- L6 3 DUP REM L5 (4 DUPLICATES REMOVED)
- L7 778 S (MODIFIED OR ALTERED) (5A) TROPISM
- L8 85 S L3 AND L7
- L9 31121 S LIPOPROTEIN(W) RECEPTOR
- L10 0 S L8 AND L9
- L11 44 S L3(P)L9
- L12 23 DUP REM L11 (21 DUPLICATES REMOVED)
- L13 71 DUP REM L1 (98 DUPLICATES REMOVED)

=> d au ti so pi 1-3 16

- L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
- IN Zlokovic, Berislav V.; Wu, Zhenhua; Deane, Rashid
- TI Therapy of Alzheimer neurovascular dysfunction by transfer of GAX to promote angiogenesis, suppress apoptosis and increase low d. lipoprotein receptor-related protein 1
- SO PCT Int. Appl., 56pp.

CODEN: PIXXD2

	PATENT NO.					KIND DATE			APPLICATION NO.						DATE			
ΡI	-							0070215 WO 2006-US30148							20060803			
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	US 20090181911					AI		2009	0 / 1 0	US 2008-988999						20080318		

- L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
- IN Betz, Ulrich; D'Urso, Donatella; Gatsios, Petros; Seewald, Michael; Strayle, Jochen; Van Es, Helmuth Hendrikus Geradus; Van Zutphen, Marlijn; Mesic, Emir
- TI Novel protein targets and methods of screening for compounds useful in treatment of cardiovascular disorders, dyslipidemia and atherosclerosis
- SO PCT Int. Appl., 136pp.

CODEN: PIXXD2

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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
ΡI	WO 2006092209	A1	20060908	WO 2006-EP1451	20060217		

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L6 ANSWER 3 OF 3 MEDLINE on STN

DUPLICATE 1

- AU Loiler S A; Conlon T J; Song S; Tang Q; Warrington K H; Agarwal A; Kapturczak M; Li C; Ricordi C; Atkinson M A; Muzyczka N; Flotte T R
- TI Targeting recombinant adeno-associated virus vectors to enhance gene transfer to pancreatic islets and liver.
- SO Gene therapy, (2003 Sep) Vol. 10, No. 18, pp. 1551-8. Journal code: 9421525. ISSN: 0969-7128.

=> d au ti so pi 1-23 112

L12 ANSWER 1 OF 23 MEDLINE on STN

DUPLICATE 1

- AU Craig Anthony T; Gavrilova Oksana; Dwyer Nancy K; Jou William; Pack Stephanie; Liu Eric; Pechhold Klaus; Schmidt Michael; McAlister Victor J; Chiorini John A; Blanchette-Mackie E Joan; Harlan David M; Owens Roland A
- TI Transduction of rat pancreatic islets with pseudotyped adeno-associated virus vectors.
- SO Virology journal, (2009) Vol. 6, pp. 61. Electronic Publication: 2009-05-18.

Journal code: 101231645. E-ISSN: 1743-422X. Report No.: NLM-PMC2687429.

- L12 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
- AU Craig, Anthony T.; Gavrilova, Oksana; Dwyer. Nancy K.; Jou, William; Pack, Stephanie; Liu, Eric; Pechhold, Klaus; Schmidt, Michael; McAlister, Victor J.; Chiorini, John A.; Blanchette-Mackie, Joan E.; Harlan, David M.; Owens, Roland A.
- TI Transduction of rat pancreatic islets with pseudotyped adeno-associated virus vectors
- SO Virology Journal (2009), 6, No pp. given CODEN: VJIOA4; ISSN: 1743-422X URL: http://www.virologyj.com/content/pdf/1743-422x-6-61.pdf
- L12 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
- IN Zlokovic, Berislav V.; Wu, Zhenhua; Deane, Rashid
- TI Therapy of Alzheimer neurovascular dysfunction by transfer of GAX to promote angiogenesis, suppress apoptosis and increase low ${\tt d.}$ lipoprotein receptor-related protein 1
- SO PCT Int. Appl., 56pp.

CODEN: PIXXD2

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US 20090181911
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- L12 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
- AU Hu, Chang-Ping; Dandapat, Abhijit; Liu, Yong; Hermonat, Paul L.; Mehta, Jawahar L.
- TI Blockade of hypoxia-reoxygenation-mediated collagen type I expression and MMP activity by overexpression of TGF- $\beta1$ delivered by AAV in mouse cardiomyocytes
- SO American Journal of Physiology (2007), 293(3, Pt. 2), H1833-H1838 CODEN: AJPHAP; ISSN: 0002-9513
- L12 ANSWER 5 OF 23 MEDLINE on STN DUPLICATE 2
- AU Tanigawa Hiroyuki; Billheimer Jeffrey T; Tohyama Jun-ichiro; Zhang YuZhen; Rothblat George; Rader Daniel J
- TI Expression of cholesteryl ester transfer protein in mice promotes macrophage reverse cholesterol transport.
- SO Circulation, (2007 Sep 11) Vol. 116, No. 11, pp. 1267-73. Electronic Publication: 2007-08-20. Journal code: 0147763. E-ISSN: 1524-4539.
- L12 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
- AU Xu, Yongping; Zhang, Muxun; Yuan, Gang
- TI Construction of recombinant adeno-associated virus expressing human full-length very low-density lipoprotein receptor gene
- SO Huazhong Keji Daxue Xuebao, Yixueban (2007), 36(6), 791-794 CODEN: HKDXBU; ISSN: 1672-0741
- L12 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
- IN Bowles, Dawn E.; Li, Chengwen; Rabinowitz, Joseph E.; Grieger, Josh; Agbandje-McKenna, Mavis; Samulski, Richard Jude
- TI Viral vectors with enhanced transduction properties comprising a chimeric adeno-associated virus (AAV) capsid, and therapeutic uses
- SO PCT Int. Appl., 81 pp.

CODEN: PIXXD2 PATENT NO. KIND DATE APPLICATION NO. DATE _____ ____ _____ ______ _____ WO 2006066066 A2 20060622 WO 2005-US45552 20051215 PΙ WO 2006066066 А3 20060810 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

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                                20081030
                                           US 2007-793430
                                                                    20070822
L12 ANSWER 8 OF 23 MEDLINE on STN
                                                        DUPLICATE 3
     Li Dayuan; Liu Yong; Chen Jiawei; Velchala Neelima; Amani Fariba;
     Nemarkommula Aravind; Chen Kui; Rayaz Hassan; Zhang Dazhi; Liu Hongmei;
     Sinha Anjan K; Romeo Francesco; Hermonat Paul L; Mehta Jawahar L
     Suppression of atherogenesis by delivery of TGFbeta1ACT using
     adeno-associated virus type 2 in LDLR knockout mice.
     Biochemical and biophysical research communications, (2006 Jun 9) Vol.
     344, No. 3, pp. 701-7. Electronic Publication: 2006-04-19.
     Journal code: 0372516. ISSN: 0006-291X.
L12 ANSWER 9 OF 23
                      MEDLINE on STN
                                                         DUPLICATE 4
     Liu Yong; Li Dayuan; Chen Jiawei; Xie Jin; Bandyopadhyay Sarmistha; Zhang
     Dazhi; Nemarkommula Aravind R; Liu Hongmei; Mehta Jawahar L; Hermonat Paul
     Inhibition of atherogenesis in LDLR knockout mice by systemic delivery of
     adeno-associated virus type 2-hIL-10.
     Atherosclerosis, (2006 Sep) Vol. 188, No. 1, pp. 19-27. Electronic
     Publication: 2005-11-21.
     Journal code: 0242543. ISSN: 0021-9150.
L12 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
     Warrington, Kenneth H.; Opie, Shaun R.; Muzyczka, Nicholas
     Improved recombinant adeno-associated virus (rAAV) expression systems for
     genetic modification of specific capsid proteins and therapeutic
     applications
     PCT Int. Appl., 180 pp.
     CODEN: PIXXD2
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    WO 2004027019
                        A2 20040401 WO 2003-US13583
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AT 405295 T 20080915 AT 2003-786493
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AU 2004226961 A1 20041118 AU 2004-226961
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                         A1 20090424 HK 2005-104362 20050524
A1 20060427 US 2005-513059 20051002
A1 20060504 US 2005-513348 20051017
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      US 20090149414
L12 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5
      Zhong, Shumei; Sun, Shihua; Teng, Ba-Bie
      The recombinant adeno-associated virus vector (rAAV2)-mediated
      apolipoprotein B mRNA-specific hammerhead ribozyme: A self-complementary
      AAV2 vector improves the gene expression
      Genetic Vaccines and Therapy (2004), 2, No pp. given
      CODEN: GVTEBH; ISSN: 1479-0556
      URL: http://www.gvt-journal.com/content/pdf/1479-0556-2-5.pdf
     ANSWER 12 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
     Loiler, Scott A.; Flotte, Terence R.; Muzyczka, Nicholas; Atkinson, Mark
      Improved rAAV vectors for enhancing transduction of cells expressing
      low-density lipoprotein receptors and therapeutic uses thereof
      PCT Int. Appl., 214 pp.
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A1 20061228 US 2005-511914 20050906
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L12 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN

Xiao, Weidong; Hauck, Bernd

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Methods and compositions for the production of chimeric adeno-associated
ТΤ
    virus (AAV) vectors with broad tissue tropism, and methods of use for gene
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- ANSWER 14 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
- Gao, Guangping; Wilson, James M.; Alvira, Maricio
- ΤI Method of detecting and/or identifying adeno-associated virus (AAV) sequences and isolating novel AAV sequences
- SO Eur. Pat. Appl., 419 pp.

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AT 317916

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- Adeno-associated virus type 2 (AAV AB -2) is a vector that shows great promise for many gene therapy protocols due to its robust nature and wide tropism. The principle AAV-2 $\,$ receptors have been identified as heparan sulphate proteoglycan (HSPG) and basic fibroblast growth factor receptor (b-FGFR). AAV-2 shows poor tropism to haematopoietic cells due in part to a lack of these receptors. In order to improve the affinity of AAV-2 for these tissues, we attempted to modify its tropism by targeting it to low density lipoprotein receptor (LDL-R) which is present on normal and leukaemic haematopoietic progenitor cells. LDL-R is a member of a class of molecules that carry ligands into cells after clustering into clathrin coated pits and has a very high binding affinity for, and a rapid internalisation of, its ligands. The identification of the optimised peptide sequence RHLRKLRKRLAR from one of the ligands of LDL-R, apolipoprotein E, has provided us with a model system to assess whether it is possible to modify the tropism of AAV-2. We have inserted oligonucleotides that encode the RHLRKLRKRLAR peptide into different regions of the VP1 gene. Using these mutated VP1 genes we have made seven different targeted recombinant AAV-2 viruses containing the cDNA for green fluorescent protein ((GFP) (trAAV-GFP)) some of whose titres are identical to that of normal recombinant AAV-2. The monocytic leukaemia cell line U937 is refractory to infection by normal recombinant AAV-GFP and expresses LDL-R. We have shown that the targeted viruses are able to deliver GFP DNA in a virion dependent manner to U937 cells, enhancing the susceptibility of these cells by at least 4 orders of magnitude. These results suggest that by using LDL-R re-targeted virus it should be possible to transduce early haematopoietic progenitor cells.
- ANSWER 19 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN

 The present invention refers to vectors derived form recombinant Adeno-associated virus (AVV) which comprise at least one selected transgene between the sequences of the 5' and 3' inverted terminal repeats (ITRs) from AAV, and a DNA sequence encoding one or more AAV Rep protein, or a fragment or a derivative thereof, outside of the context of the AAV ITRs. These vectors have a larger packaging capacity and prior art vectors. The vectors according to the invention are useful in gene therapy. Thus,

plasmid pITR(GFP-Neo)P5Rep was prepared and HeLa cells were transfected with it. This plasmid contains the GFP gene under control of the CMV early promoter and the neomycin resistance gene under control of the SV40 early promoter between the 3'- and 5'-ITRs and the Rep gene controlled by the P5 and P19 promoters outside of the ITRs. The ITR-flanked expression construct was inserted into the HeLa cell genome in a Rep-dependent manner at the aavs1 site.

- L12 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
- Provided are methods for selectively expressing therapeutic mols., such as secretory proteins, antisense mols. and ribozymes, in the liver. The methods find use in treating hepatic diseases or conditions. The methods also find use in treating any disease or condition in which systemic administration of the therapeutic substance, for example, a secretory protein, is desired. The methods involve administering to a mammalian patient having a need for liver expression of a therapeutic mol. an AAV vector containing a therapeutically effective amount of the therapeutic mol. Also provided are novel vectors employable in these methods. Expts. revealed that, following i.v. injection of AAV vectors into mice, the AAV genomes were found predominantly in the liver. The heterologous genes carried by these vectors (chimeric cytomegalovirus promoter-lacZ or β -globin promoter-globin genes) were expressed in the liver. Cotransfection of adenovirus 2-infected 293 cells with the AAV vectors and helper plasmid containing cap and rep genes resulted in production of 0.1-10% wild-type AAV. Replacement of the last 10 nucleotides of the ITR D sequence with unrelated nucleotides reduced this illegitimate recombination was reduced. Four recombinant AAV vectors (pD-5, pD-10, pD-15 and pD-20) with such modified ITR regions were prepared
- L12 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
- AB The invention relates to the use of AAV vectors for the transfer of genes to the heart and vasculature. The vector preferably contains a gene encoding a protein which improves heart and vascular function during heart failure. In a specific embodiment, the vector is introduced into the heart and vasculature via a catheter, with the aid of fluoroscopy. The method and vectors for use therein provide for safe and stable gene expression of the transferred genes.

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